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EXAMINER

SCHNIZER, RICHARD A

ART UNIT

PAPER NUMBER

1635

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18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

09/806,080

JOMAA, HASSAN

Examiner

Art Unit

Richard Schnizer, Ph. D

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 19 May 2003.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-8, 18, 22, 24 and 25 is/are pending in the application.
- 4a) Of the above claim(s) 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 3-8, 22, 24 and 25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 17.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

Priority

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country. Although Applicant has submitted priority documents DE 19843279.8 and DE 19923567.8, the executed declaration does not claim priority to these documents. Also, a certified translation of these documents has not been filed.

Claim Objections

Claims 5 and 22 are objected to because they depend from cancelled claim 1. For the purpose of examination, claims 5 and 22 have been considered to depend from claim 3.

Specification

Previously the specification was objected to because it contains two page 1s, with the second page 1 consisting of a translator's comment followed by a description of the gcpE protein. The Examiner has deleted the translator's comment and has renumbered the pages consecutively. A substitute specification was received in Paper No. 16, however, this specification was not entered because it differed from the originally filed specification by omitting information present at page 3, lines 14-17 and 23-27 and page 4, lines 1 and 2.

The specification is objected to because at page 1, lines 25 and 26 it refers to "Figure 1". However, the specification as filed did not contain any Figures.

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 3-8, 18, 22, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3-8, 22, 24, and 25 have been amended to recite "SEQ ID NO:6 with conservative amino acid substitutions". The specification as filed provides no support for the phrase "conservative amino acid substitutions" or the scope of amino acids substitutions implied by this phrase. The only support in the specification for altering SEQ ID NO:6, appears to occur at the sentence bridging pages 3 and 4. This passage supports variants of SEQ ID NO:6 in which one or more amino acids have been deleted, added or replaced by other amino acids, wherein the catalytic function of the polypeptide is retained. The phrase conservative amino acid substitutions does not appear in the specification, and could be reasonably construed by one of skill in the art to include substitutions that maintained some structural feature of the enzyme without regard to the catalytic function of the enzyme. In other words, a conservative substitution could be construed as one that eliminates catalytic activity without destroying the three-dimensional structure of the overall enzyme. This reasonable interpretation of the phrase is not supported by the specification, so the phrase "conservative amino acid substitutions" represents new matter.

Enablement

Claims 3-8, 18, and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for such nucleic acids encoding gcpE proteins known in the prior art as detailed below, does not reasonably provide enablement for SEQ ID NO:6, or for any other analogue or derivative of SEQ ID NO:6, nor does it provide enablement for any 3' untranslated sequence that effects the addition of poly(A) in prokaryotes or viruses. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Nature of the invention

The claims are drawn to nucleic acids encoding SEQ ID NO:6 or SEQ ID NO:6 with conservative substitutions, to host cells and organisms comprising the nucleic acids, to a method of making the host cells and organisms, and to a method of producing SEQ ID NO:6 or SEQ ID NO:6 with conservative substitutions. SEQ ID NO:6 is asserted to encode the gcpE protein of *P.falciparum*. The specification teaches that the claimed nucleic acids can be used in the expression and purification of gcpE, that gcpE is involved in the synthesis of isoprenoids by a non-mevalonate pathway (DOXP pathway), and that nucleic acids encoding gcpE can be used for the purpose of producing isoprenoids. See e.g. page 1, lines 31 28-31; page 5, lines 25-32; page 9, lines 20-22, page 10, lines 8-11, and page 12, lines 13-26. The specification asserts that gcpE is a kinase that will catalyze phosphorylation of any one of a number of substrates listed at page 2 of the specification.

Breadth of the claims

The claims embrace any nucleic acid encoding SEQ ID NO:6 or encoding a polypeptide that differs from SEQ ID NO:6 by any number of conservative mutations. The claims do not require that the enzyme should have any activity.

Guidance in the specification

The specification fails to define what exactly constitutes a conservative substitution. The specification fails to teach how to use a polypeptide that has no activity, and provides no guidance as to what residues of SEQ ID NO:6 can be altered to provide a polypeptide that retains any catalytic activity. The specification fails to teach what enzymes, other than DOXP synthase, DOXP reductoisomerase, and gcpE are required for the synthesis of isoprenoids by the DOXP pathway.

Examples in the specification

The specification teaches no working examples of the invention, in particular, no evidence is provided for any kinase activity of SEQ ID NO:6 or its analogues.

State of the prior art and predictability of the art.

A search of the prior art showed only two proteins of known sequence having gcpE function. See Rather et al (J. Bact. 179(7): 2267-2273, 4/1997, abstract). The most closely related of these sequences was only 10% identical to SEQ ID NO:6. See sequence alignment attached to Paper No. 14. Baker et al (FEMS Microbiol. Lett. 94(1-2): 175-180, 1992) taught that the E.coli gcpE gene encoded a protein of unknown function (see abstract). Rather (1997) taught that E.coli gcpE was able to functionally complement aarC1 of P.stuartii in its roles as a negative regulator of the aac(2') gene. Neither of these publications provides any evidence to support any kinase activity of gcpE, and there is no evidence in the prior art of record that provides any support for the identification of gcpE as a kinase. In fact the catalytic activity of gcpE was unknown to those of skill in the art as late as December of 2001 (see McAt er et al (J. Bact.

183(24): 7403-7407, 12/2001, especially abstract). While it was known in the art at the time of filing that isoprenoid biosynthesis occurred in some organisms by the DOXP pathway, it is apparent from the priority document DE 198 43 279.8 that at the time of filing, all of the enzymes required for isoprenoid synthesis in the DOXP pathway were not known. See Fig. 7. In fact, Applicant admits in the sentence bridging pages 9 and 10 of Paper No. 16, that the terminal biosynthetic steps of the DOXP pathway have not been elucidated, and it is also apparent from Fig. 4 on page 7405 of McAteer (2001) that number and identity of enzymes required for the DOXP pathway remained unknown after the time the invention was filed. Subsequent to the time of filing, Hecht et al (PNAS 98(26): 14837-14832, 12/2001) showed that *E.coli* gcpE catalyzes the interconversion of 2C-methyl-D-erythritol 2,4-cyclodiphosphate into 1-hydroxy-2-methyl-2-(E)-butenyl 4-diphosphate. Note that this is not a phosphorylation reaction. Thus it is apparent that gcpE does not encode a kinase, and that at the time of filing one of skill in the art did not know all the enzymes that were required to synthesize isoprenoids by the DOXP pathway, such that one could not reconstruct the pathway by expressing genes encoding its component enzymes. Furthermore, SEQ ID NO:6 is not more than about 10% identical to any protein identified in the prior art as a gcpE protein, so it is highly unpredictable as to whether or not SEQ ID NO:6 encodes a polypeptide that could function as a gcpE, and it is highly unpredictable as to whether nucleic acids encoding SEQ ID NO:6 could be used to complement a gcpE deficiency in any organism, i.e. it is unpredictable as to whether SEQ ID NO:6 could be used to allow *E.coli* strains lacking endogenous gcpE to produce isoprenoids. See discussion of the relationship of protein structure to function below and in Paper No. 14. For these reasons one of skill in the art, relying on the teachings of the specification and the prior art, would have had to perform undue experimentation to use the claimed invention to express a kinase, or to

use the claimed invention to synthesize isoprenoids, such that one of skill in the art could not have used the claimed invention as intended without undue experimentation.

Even if Applicant is able to provide objective evidence that SEQ ID NO:6 encodes a kinase, the specification provides no guidance as to what conservative substitutions of SEQ ID NO:6 will provide an enzyme that can be used as taught in the specification, i.e. for the production of isoprenoids. The prior art teaches that, at the time the invention was made, the effects of amino acid substitutions and deletions on protein function were highly unpredictable. Rudinger (In Peptide Hormones J.A. Parsons, Ed. University Park Press, Baltimore, 1976, page 6) teaches that "[t]he significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study." Furthermore Ngo et al (In The Protein Folding Problem and Tertiary Structure Prediction, K. Merz Jr. and S. Legrand, Eds. Birkhauser, Boston, 1994, see page 492) teaches that "[i]t is not known if there exists an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. Decades of research have failed to produce such an algorithm". For further evidence of the unpredictability of protein structure and function relationships, see also Gerhold et al.[BioEssays, Volume 18, Number 12, pages 973-981(1996)]; Wells et al. [Journal of Leukocyte Biology, Volume 61, Number 5, pages 545-550 (1997)]; and Russell et al.[Journal of Molecular Biology, Volume 244, pages 332-350 (1994)]. One might argue that it would not be undue experimentation to express and assay polypeptides individually, and thereby empirically determine the function of each one. However as set forth in *In Re Fisher*, 166 USPQ 18(CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with the degree of unpredictability of the factors involved.

In view of the lack of evidence in the specification and the prior art supporting Applicant's assignment of a kinase function to gcpE, and the assignment to gcpE of a non-kinase activity in both the prior art and the post filing art, there is reason to doubt that SEQ ID NO:6 encodes a kinase, and it is totally unpredictable as to what alterations to SEQ ID NO:6 would produce kinase activity, short of substituting the sequence of a known kinase for that of SEQ ID NO:6.

Claims 5 and 22 explicitly require a 3' untranslated sequence that results in the addition of poly(A) residues in prokaryotes, viruses, and eukaryotes. However, one of ordinary skill in the art appreciates that viruses and prokaryotes do not perform, poly(A) addition. This is a process that is performed only in eukaryotes. While viral RNAs may acquire poly(A) tails, this does not happen in a virus, as required by the claims, rather it happens only in infected eukaryotic cells because the mechanism for making it happen exists only in eukaryotes. Hence, there is no such thing as a 3' untranslated sequence that results in the addition of poly(A) residues in prokaryotes and viruses. See for example, Campbell (*In Biology*, Fourth Edition, The Benjamin Cummings Publishing Company, Inc, page 314-315.

Because there is reason to doubt the objective accuracy of the specification's assertion that SEQ ID NO:6 encodes a kinase, and in light of the unpredictable nature of protein structure/function relationships and the lack of guidance or examples in the specification in this regard, one of skill in the art would not be able to make or use the invention to phosphorylate the substrates listed in the specification. Because the

specification fails to teach what are the necessary enzymes required to complete the DOXP pathway, one of skill in the art would have to perform undue experimentation in order to use SEQ ID NO:6, or its variants, to synthesize isoprenoids. Because neither the prior art of record nor the specification provides any example or guidance as to how to obtain a 3' untranslated sequence that results in the addition of poly(A) residues in prokaryotes and viruses, one of skill in the art could not make or use the invention as claimed without undue experimentation.

Written Description

Claims 3-8, 22, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn to a genus of nucleic acids encoding SEQ ID NO:6 or SEQ D NO:6 with "conservative substitutions". The claims require no particular activity of the protein encoded by SEQ ID NO:6, and the specification fails to define what is intended by "conservative substitutions".

The following analysis is based on the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

The following passage on the treatment of genus claims is particularly relevant.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial

variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

The specification discloses a single species of the genus of encoded polypeptides (SEQ ID NO:6), which the specification asserts to be a gcpE polypeptide. A search of the prior art showed only two proteins of known sequence having gcpE function. See Rather et al (J. Bact. 179(7): 2267-2273, 4/1997, abstract). The most closely related of these sequences was only 10% identical to SEQ ID NO:6. See enclosed sequence alignment. Clearly this is evidence of great variability within the claimed genus. However, if one considers that the genus includes all polypeptides that can be derived from SEQ ID NO:6 by conservative substitution without regard for the function of the polypeptide, then the variability within the genus would be even greater.

Having established that the claimed genus comprises substantial variability, and that the relationship between protein structure and function is unpredictable (see above under enablement), it is clear that the specification fails to provide an adequate written description of the claimed genus, because the Guidelines on Written Description state that "[i]n an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. So, one of skill in the art could not conclude that Applicant was in possession of the claimed invention at the time of filing.

Response to Arguments

Regarding the enablement rejection, Applicant argues at page 8 of the response that limitation of the claims to nucleic acids that encode SEQ ID NO:6 or SEQ ID NO:6

with conservative substitutions should overcome the portion of the enablement rejection formerly devoted to "analogs" of SEQ ID NO:6. Applicant submits that "one of skill in the art would know that a conservative substitution includes replacement of one amino acid residue with a different residue having similar biochemical characteristics, e.g. valine for glycine, arginine for lysine etc)." This argument is unpersuasive because it is unsupported by evidence. The evidence of record as set forth in Rudinger (1976), Ngo (1994), Gerhold (1996), Wells (1997), and Russell (1994) is that the effects of amino acid substitutions on protein structure are highly unpredictable. Applicant has presented no evidence or logic to the contrary.

Regarding the written description rejection, Applicant appears to argue at pages 9 and 10 of the response that, because the post-filing art (Altincicek (2001)) shows that *E.coli gcpE* is involved in the DOXP pathway, the instantly claimed sequences have an indispensable and credible role in the isoprenoid biosynthesis, and therefore Applicant was in possession of the claimed genus of sequences. This argument is unpersuasive because it merely presents evidence supporting the variability within the claimed genus. As noted in the rejection, *E.coli gcpE* is only about 10% identical to SEQ ID NO:6. It follows that if SEQ ID NO:6 is a *gcpE*, then there is tremendous variability within the genus (only 10% identity, and perhaps less). The rejection establishes that the relationship between protein structure and function is unpredictable. The Guidelines on Written Description state that "[i]n an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. Applicant has not provided any evidence or reasoning to indicate what feature of SEQ ID NO:6 is representative of the members of the claimed genus, so one of skill in the art could not conclude that Applicant was in possession of the claimed invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-8, 22, 24, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-8, 22, 24, and 25 are indefinite because it is unclear what is intended by "conservative amino acid substitutions". The specification does not define this phrase and there is no single art-recognized definition.

Claims 6 and 22 are indefinite they recite "the genome" without antecedent basis. It is noted that viruses, eukaryotes, and prokaryotes generally have distinct genomes, so it is unclear to what genome the claims refer. Note that "viruses, eukaryotic cells, prokaryotic cells, plant, and plant cells" are not recited as alternatives, therefore the claims as written require that viruses, eukaryotic cells, prokaryotic cells, plant, and plant cells must all have one and the same genome.

Claim 7 is indefinite because it recites "which sequences" without proper antecedent basis. Claim 3, from which claim 7 depends is drawn to an "isolated nucleic acid comprising a sequence". Instant claim 7 refers to more than one sequence, i.e. "which sequences", so it is unclear to what sequence claim 7 refers.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3, 4, 6-8, 22, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Rather et al (J. Bact. 79(7): 2267-2273, 4/1997).

Rather taught an expression construct encoding *E.coli gcpE*, and a transgenic bacterium (*P.stuartii*) comprising the construct, and a process for making the bacterium. See abstract, particularly lines 10-12, Fig. 2 on page 2270, and lines 1-3 of paragraph bridging columns 1 and 2 on page 2271. Because *E.coli gcpE* functions in the *E.coli* DOXP pathway, it is considered to be a form of SEQ ID NO:6 comprising conservative substitutions that preserve the essential function of *gcpE* in a DOXP pathway.

Thus Rather anticipates the claims.

Response to Arguments

Applicant argues at page 12 of the response that Rather does not teach a version of SEQ ID NO:6 with conservative amino acid substitutions or a sequence that would be useful in the DOXP pathway. These arguments are unpersuasive because they lack evidentiary or logical support. It appears that Applicant has overlooked lines 10-12 of the abstract, as well as Fig. 2 on page 2270, and lines 1-3 of paragraph bridging columns 1 and 2 on page 2271 which clearly show that Rather teaches an isolated nucleic acid encoding an *E.coli gcpE* protein. Evidence that the protein is functional is given at Fig. 4, and page 2272, column 1, lines 15-17. Usefulness in the DOXP pathway, while not required by the claims, is inherent in the function of *E.coli gcpE*, so arguments that Rather fails to teach a sequence that would be useful in the DOXP pathway are both misplaced and incorrect. Applicant appears to argue that because *E.coli gcpE* protein is functionally equivalent to *P.stuartii aarC* protein, it cannot be

functionally equivalent to *P.falciparum* gcpE. This argument lacks any basis in fact or logic. For example, Applicant has not shown that *P.stuartii* aarC protein does not function in a DOXP pathway, so it is not logical to assume that it is not functionally equivalent to *P.falciparum* gcpE. On the other hand, in the case that *P.stuartii* aarC protein does not function in a DOXP pathway, Applicant has not eliminated the possibility that *E.coli* gcpE could have more than one function, i.e. that it functions in the DOXP pathway as well as in some other non-DOXP pathway in which *P.stuartii* aarC protein also functions.

For these reasons the rejection is maintained.

Conclusion

No claim is allowed.

Claims 5 and 25 are free of the prior art of record.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

This application contains claim 18 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.



SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER